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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,275	08/24/2001	Christopher P. Adams	EXT-062CN	3814

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	15

DATE MAILED: 02/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/939,275	Adams
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *6/24/01 and 11/25/02* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Sequence Rules

1. This application complies with the Sequence Rules and the sequences were entered by the Scientific and Technical Information Center.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 5, 7, and 19 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Jiro et al (JP H3[1991]-47097) (February 28, 1991) in view of Gelfi et al (Biotechniques (November 1996) 21:926-32).

Jiro et al expressly teaches a method for purifying nucleic acid target molecules from a reaction using a purification device comprising the following steps:

(a) introducing the primer extension sequencing reaction mixture into a purification device comprising an electrophoretic medium, wherein the electrophoretic medium contains immobilized nucleic acid capture probes (Page 6, lines 12-18);

(b) subjecting the electrophoretic medium of step (a) to an electric field resulting in the electrophoretic migration of one, or more, target molecules into at least one region of the electrophoretic medium containing immobilized capture probes, wherein the target molecules bind to immobilized capture probes (Page 6, lines 18-20);

e) collecting the target molecules (Page 6, lines 20-24).

Jiro et al. does not expressly teach the step of imposing conditions on the electrophoretic medium that dissociate the targets and their complementary capture probes.

Gelfi teaches a method of increasing a thermal gradient to cause denaturation of hybridization complexes by increasing the voltage of the gel (abstract and page 926, column 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the use of increasing voltage for a separate heating element as taught by Jiro et al. in order to cause denaturation, since Gelfi states "Additionally, the denaturing thermal gradient is not controlled externally, but generated internally by Joule heat produced by voltage ramps (page 926, abstract)". With regard to the use of increased voltage to dissociate the hybridization complex, Jiro et al. expressly teaches the use of

increasing temperature to effect the dissociation of the hybridization complex. Jiro et al. uses a separate and external heating source to effect this increased temperature (page 9). Gelfi recognizes Joule's law of electricity which teaches that heat generated in the electrical system is directly proportional to the square of intensity of current which, in turn, is directly proportional to the voltage of the electrical system. Therefore, when Jiro et al. teaches the release of nucleic acids by increasing the temperature, it would have been immediately and prima facie obvious to the ordinary practitioner to substitute the method of Gelfi with the simple use of increasing voltage to increase the temperature of the gel, which serves to minimize the different apparatuses needed to perform the denaturation function, thereby saving material expense, time and effort.

4. Claims 2-4, 10-14, and 16 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Jiro et al (JP H3[1991]-47097) (February 28, 1991) in view of Gelfi et al (Biotechniques (November 1996) 21:926-32) further in view of Cantor et al (U.S. Patent 5,482,836) (January 09,1996).

Jiro et al. in view of Gelfi expressly teach the methods of claims 1, 5, 7, and 19 for purifying target molecules as described above.

Jiro et al. in view of Gelfi do not teach the method of multiplexing the assay, such as by use of microtiter plates selected from the group consisting of 6, 12, 48, 96, and 384.

Cantor et al. teaches multiplexing the assay by using the microtiter plates which are available in the market as 6 well to 96 well plates as the purification device (Column 7, lines 65-66).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method of multiplexing the assay by using the microtiter plates which are available in the market as 6 well to 96 well plates as the purification device of Cantor et al. in the method of Jiro et al. in view of Gelfi since Cantor et al. states, "Another interesting variation of this invention would be multiplexing or using two or more different traps so as to isolate two or more different targets from a single mixture (Column 12, lines 45-47)". An ordinary practitioner would have been motivated to substitute and combine the method of multiplexing the assay by using the microtiter plates which are available in the market as 6 well to 96 well plates as the purification device of Cantor et al. in the method of Jiro et al. in view of Gelfi in order to achieve the express advantages, as noted by Cantor et al., of an invention which provides multiplexing or using two or more different traps so as to isolate two or more different targets from a single mixture.

5. Claims 8, 9, 17, and 18 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Jiro et al (JP H3[1991]-47097) (February 28, 1991) in view of Gelfi et al (Biotechniques (November 1996) 21:926-32) further in view of Cantor et al (U.S. Patent 5,482,836) (January 09,1996) further in view of Mullis (U.S. Patent 4683202) (July 28, 1989).

Jiro et al. in view of Gelfi further in view of Cantor et al expressly teach the methods of claims 1, 5, 7, 19, 2-4, 10-14, and 16 for purifying target molecules as described above.

Jiro et al. in view of Gelfi further in view of Cantor et al do not teach the method of extension of primers to form complementary primer extension products which act as templates for synthesizing the desired nucleic acid sequence.

Mullis teaches the method of extension of primers to form complementary primer extension products which act as templates for synthesizing the desired nucleic acid sequence (Column 4, line 15 to Column 15, line 42).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method of extension of primers to form complementary primer extension products which act as templates for synthesizing the desired nucleic acid sequence of Mullis in the method of Jiro et al. in view of Gelfi further in view of Cantor et al. since Mullis states, "The present invention may be useful not only for producing large amounts of an existing nucleic acid or completely specified sequence, but also for producing nucleic acid sequences which are known to exist but are not completely specified (Column 3, lines 19-23)". An ordinary practitioner would have been motivated to substitute and combine the method of extension of primers to form complementary primer extension products which act as templates for synthesizing the desired nucleic acid sequence of Mullis in the method of Jiro et al. in view of Gelfi further in view of Cantor et al. in order to achieve the express advantages, as noted by Mullis, of an invention which may be useful not only for producing large amounts of an existing nucleic acid or completely specified sequence, but also for producing nucleic acid sequences which are known to exist but are not completely specified.

6. Claims 6 and 15 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Jiro et al (JP H3[1991]-47097) (February 28, 1991) in view of Gelfi et al (Biotechniques (November 1996) 21:926-32) further in view of Stamato et al (U.S. Patent 4,830,726) (May 16, 1989).

Jiro et al. in view of Gelfi expressly teaches the methods of claims 1, 5, 7, and 19 for purifying target molecules as described above.

Jiro et al. in view of Gelfi do not teach reversing the polarity of the electric field, wherein the released target molecule will migrate back toward the test sample receptacle and wherein it is subject to collection.

Stamato et al teaches the method of separating DNA molecules by gel electrophoresis which employs alternate applications of high and low strength electric fields in opposite directions to a gel matrix containing DNA (Column 7, line 59 to Column 10, line 13).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the separation of DNA molecules in alternating asymmetric electric fields method of Stamato et al in the purification method of Jiro et al. in view of Gelfi since Jiro expressly teaches the "forced movement of DNA fragment sample within the electrophoretic carrier by means of electrophoresis which permits hybridization reaction to take place more rapidly, and the reaction to be completed in shorter time, than would be the case were it to undergo passive diffusion as in the conventional method employing a nitrocellulose membrane. Furthermore, the instant invention permits easy removal, by means of electrophoresis, without employment of washing operations involving filling and discharge solutions and so forth,

of the sample that does not bind or binds weakly during the hybridization reaction (Page 11, lines 29-38)." The ordinary practitioner would have combined this concept with that of Stamato, since Stamato et al states with regard to the polarity reversal method that, "one of skill in the art will acknowledge the applicability of this method to DNA from a variety of sources, other compositions appropriate for electrophoretic separation, and for a variety of known uses of an electrophoretic methods (Column 7, lines 27-32)." An ordinary practitioner would have been motivated to combine the teachings of Jiro et al. in view of Gelfi with those of Stamato et al. for the stated and expected benefits of increasing the ability of separating nucleic acid of broad size range as Stamato states, "The advantages offered by the method of the present invention include the ability to separate molecules from about 0.15 to about 2000 Kb (Column 3, lines 20-22)".

7. Claim 20 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Jiro et al (JP H3[1991]-47097) (February 28, 1991) in view of Gelfi et al (Biotechniques (November 1996) 21:926-32) further in view of Ghosh et al. (U.S. Patent 5,478,893) (December 26, 1995).

Jiro et al. in view of Gelfi expressly teach the methods of claims 1, 5, 7, and 19 for purifying target molecules as described above.

Jiro et al. in view of Gelfi do not teach the method wherein the capture probes are immobilized in the electrophoretic medium by copolymerizing the 5'-acrylamide moiety with the electrophoretic medium.

Ghosh et al. teach the method wherein the capture probes are immobilized in the electrophoretic medium by copolymerizing the 5'-acrylamide moiety with the electrophoretic medium (Abstract and Examples 1-6 and claims 1-22).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method wherein the capture probes are immobilized in the electrophoretic medium by copolymerizing the 5'-acrylamide moiety with the electrophoretic medium of Ghosh et al in the method of Jiro et al. in view of Gelfi since Ghosh et al states, "This results in immobilized oligonucleotides that exhibit superior direct capture ability for complementary oligonucleotides, double stranded DNA, and sandwich hybridization (Column 3, lines 37-40)". An ordinary practitioner would have been motivated to substitute and combine the method wherein the capture probes are immobilized in the electrophoretic medium by copolymerizing the 5'-acrylamide moiety with the electrophoretic medium of Ghosh et al in the method of Jiro et al. in view of Gelfi in order to achieve the express advantages, as noted by Ghosh et al., of a method which provides immobilized oligonucleotides that exhibit superior direct capture ability for complementary oligonucleotides, double stranded DNA, and sandwich hybridization.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner

February 11, 2003

ARUN K. CHAKRABARTI
PATENT EXAMINER